Relapse rates in patients (pts) after autologous stem cell transplant (SCT) for high risk or refractory NHL remains high. Our preclinical studies showed that activated T cells (ATC) armed with anti-CD3 x anti-CD20 bispecific antibody (CD20Bi) lyse rituximab-resistant CD20+ lymphoma cells. A phase I trial was conducted in 15 high risk or refractory NHL pts to determine the safety of armed ATC (aATC) given after SCT and whether aATC infusions accelerate immune recovery and provide an anti-lymphoma effect. Leukopheresis products were activated with anti-CD3, expanded in IL-2, armed with CD20Bi, and cryopreserved for infusions after SCT. At the time of SCT, there were 6 pts in 1st or 2nd remission (CR), 4 pts had refractory disease (PRD), 4 pts were in partial response, and 1 pt had progressive disease (PD). Pts received 5-20 $\times$ 10^9 aATC per infusion. The first 3 patients received $5x10^9$ three times per week for 3 weeks and then once per week for 6 weeks for a total aATC dose of $75x10^9$. Subsequently, the schedule was revised to 1 infusion/week for 4 weeks with infusion doses of 10, 15, and $20x10^9$ aATC. The median dose of CD34+ cells/kg infused was $4.0x10^6$(1.04-12.3x10^6). The ATC product was 92% viable, contained medians of 96.5% CD3, 67% CD4, and 48.9% CD8 cells. Fifteen pts received aATC and 12 were evaluable for toxicities. The Table 1 summarizes grade 1-3 events.

Table 1. Grade-1-3 Events

Dose	5 billion	10 billion	15 billion	20 billion
Pts Number	3	3	3	3
Infusions	15	4	4	4
Fever	3	10	12	12
Chills	2	7	3	4
Malaise	1	2	7	11
Hypotension	3	4	1	5
Tachycardia	3	2	5	4
Nause/vomiting	0	7	3	4
Headache	0	2	2	2
Dyspnea	1	0	0	0
Hypoxia	0	0	0	1

(NCI Immunotherapy Criteria).

The median day to engraftment was 14.75 days without G-CSF. aATC could be detected by flow cytometry up to 12 hours after infusion. The proportions of CD4 cells were in the normal range up to a month. There was a $>$ 4x increase in the mean ($\pm$SD) number of IFNγ EliSpots in response to Daudi cells from $30.5\pm20.5/10^6$ PBL preSCT to $125.6\pm130/10^6$PBL post SCT, $p < 0.008$. The median cytotoxicity mediated by NK cells ranged from 8.2-13.7% between 2 weeks and 3 months after SCT. Serum cytokines and chemokines peaked around 4 hrs after aATC infusions with 1-2 log increases in IL-2, IL-7, IL-15, IL-2r, MIP-1β, IP10, MIP-1α, MIG, and MICP-10. At 90 days after SCT, 9 pts were in CR and 6 pts had PD. The median OS has not been reached and OS is projected to be 55% at 4 years. Pts in CR prior to SCT had longer survival at 85% with no relapses after 1 year after SCT. These findings show that: 1) ATC can be expanded from heavily pretreated NHL pts; 2) aATC infusions are safe; 3) induce high levels of serum cytokines and chemokines; and 4) may provide anti-tumor help and cytotoxicity after SCT.

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COMBINING AZACITIDINE (VIDAZA®, AzA) AND DONOR LYMPHOCYTE INFUSIONS (DLI) AS FIRST SALVAGE TREATMENT IN PATIENTS (PTS) WITH ACUTE MYELOID LEUKEMIA (AML) OR MYELODYSPLASTIC SYNDROMES (MDS) RELAPSING AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (Allo-SCT): INTERIM-ANALYSIS FROM THE AZARELA-TRIAL (NCT-00795548)

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Prognosis for pts with AML/MDS relapsing after allo-SCT is poor and therapeutic options are limited. Results from recent retrospective analyses on the use of Aza +/- DLI in pts with AML/MDS, who relapsed after allo-SCT, were encouraging.

To evaluate the potential of Aza combined with DLI as 1st salvage therapy in pts with AML/MDS relapsing after allo-SCT we conducted a prospective phase-II multicenter trial. Pts were allowed to receive up to 8 cycles Aza (100 mg/m^2/d d1-5, every 28 d) and 3 DLI with increasing dosages ($1-5x10^6$–$1-5x10^8$ cells/kg) after every 2nd Aza cycle. So far, 25 pts (15 f/10 m) are evaluable for this analysis.

At diagnosis 23 (92%) had AML (15 de novo/8 following MDS), 1 (4%) MDS (RAEB-1) and 1 (4%) MDS/MPS (CMML-1). Based on cytogenetics 21 pts belonged to an adverse or intermediate risk group, whereas 2 pts had favorable cytogenetics (2 n.p.).

At transplant, 6 pts (24%) had induction failure, 6 (24%) suffered from 1st or 2nd relapse, 10 pts (40%) were in 1st or 2ndCR, while 3 pts (12%) were untreated. Eight pts (35%) received grafts from MSD and 15 (65%) from MUD (2 pts missing data). PBSC were used in 24 pts (96%; 1 missing). Prior to relapse 9 (36%) and 3 (12%) pts had episodes of aGvHD and/or cGvHD, respectively.

At relapse, 4 (31%) of 13 evaluable pts had normal cytogenetics, while 9 (69%) had chromosomal aberrations including 6 pts (46%) with complex karyotype. Relapse occurred in median 160 d (range 19-1199) after allo-SCT (BM blasts 34%, range 5-100%, donor chimerism 63% range 1-100%). Median age was 54 y (range 29-71). Patients received a median of 3 cycles Aza (range 1-8) and 18 pts (72%) received DLI (median: 1, range 1-4, median CD3 dose $5x10^6$/kg/DLI, range $1-207x10^6$).

Overall response rate was 64% with 5 pts (20%) achieving CR/CRi, 3 (12%) PR and 8 (32%) SD. Median response duration was 266 d. Acute GvHD occurred in 6 pts (24%) (2 skin/6 liver/ 2 gut) after a median of 65 d (range 19-179) following the 1st DLI. Three pts (12%) had limited cGvHD. Hematotoxicity III°-IV° was observed in 64%. Common adverse events were gastrointestinal side effects and infections. After a median follow-up of 100 d (range 25-485) 15 pts (60%) are alive. Median OS of all pts is 184 d (range 87-281). All pts, who achieved a CR/CRi, remained in ongoing remission for a median of 229 d.

Our data suggest that salvage therapy with Aza + DLI for pts with AML/MDS relapsing after allo-SCT is feasible and has significant anti-leukemic activity in these pts.

GRAFT PROCESSING

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A COST EFFECTIVE ANALYSIS OF A RISK-ADAPTED ALGORITHM FOR PLERIXAFOR USE IN AUTOLOGOUS PERIPHERAL BLOOD STEM CELL MOBILIZATION

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Up to 30% of patients fail to collect minimum numbers of PBSC for ASCT, and up to 50% of patients fail to collect the optimal number. Plerixafor, a CXCR4 antagonist, in combination with G-CSF has shown superior results in mobilizing PB CD34+ cells in comparison to G-CSF alone for autologous PBSC mobilization in patients with NHL or MM. However, due to its high cost, we commenced a risk adapted algorithm for the utilization of plerixafor starting in Feb 2009.

Jan-Dec 2008 was the baseline. Patients in upfront mobilization clinical trials with plerixafor were excluded. From Feb-Nov 2009, the risk adapted algorithm Plerixafor-1 was used. PBSC mobilization was commenced with G-CSF at 10 mcg/kg/day. If PB CD34 on day 4 or day 5 was $\geq$ 10/μL, apheresis was commenced the next morning.